Miscellaneous Dermatoses

1- lichen sclerosus et atrophicus → 1

2- Gireiatric dermatology

3- Atrophy of skin
   - ↳ Anetoderma
   - ↳ Striae (stretch marks)

4- perforating Dermatosis
   - kyrle's disease
   - Hyperkeratosis lenticularis perstans
   - perforating folliculitis
   - elastosis perforans
   - Colloid milium

5- Flushing

6- Histiocytoses
   - Langerhans
   - Non-langerhans
   - DD Red Face

7- primary Immunodeficency Disorders

8- السكابيز

• Lichen Sclerosus et Atrophicus •

- **D.F**: uncommon disease.
  - more in female (10:1)
  - 40 - 50 yr.
  - may develop in childhood
  - The genitals most frequent site
  - alone or ē extragenital lesion

• Clinical features:

[A] Extragenital lesions

- Rare in children
- non-Itchy, minute, Shiny Porcelin-White atrophic papules → may coalesce → to form irregular white plaque → with slight induration "Sclerosus"
- Small Comedo-like follicular plugs → seen on surface
- Rarely:- Bullae - purpura Telangectasia - milia.

- Site: - upper part of Trunk → specially Between and Below Breast - around the Neck, flexuar surface of the wrist

[B] Mouth lesions:

Reticular lesion similar to Lichen planus Bluish-white plaques: inner surface of cheek

[C] LSA of the Vulva: - "Kraurosis Vulva"

- Itchy - Sharply demarcated, whitish lesions
- in perianal Region
- The vulva and anal Region → encircled in figure of-eight pattern "Keyhole" lesion
- atrophy of Labia, narrowing of vaginal orifice
- The ptn Complain of soreness - dyspareunia
- in 20% of ptn → extragenital Cut. lesions occur.
- may occur in: - prepubertal children (confused ē sexual abuse) lesion improved by: Menarche, in contrast to lesion in adult → which progress.

*LSA is not intrinsicaly precancerous, But considered chronic Scar → continuously exposed to humid milieu (Carcinogenesis)

D LSA of glans penis + prepuce

[Balanitis Xerotica obliterans BXO]

- Ivory-white atrophic Macules on glans penis
- the pt complain of:- Itchy - Soreness priapism - phimosis
- if the prepuce is involved in uncircumcised pt → SCC may develop.
- pt ♂ genital lesion should Be seen every 6-12 ms → for early detection of SCC

• Histopathology:

① in Cutaneous LSA:

1. Hyperkeratosis with follicular plugging
2. Atrophy of St. malpighii with Hydropic degeneration of Basal cells
3. Marked edema and Homogenization of collagen in upper dermis
4. inflammatory infiltrate in mid-dermis
   - ↳ lymphoid cells intermingled with some histocytes
   - ↳ older lesion → infiltrate is absent

② in genital LSA:

- No follicular plugging D.t absence of follicles

Histopathological features of morphea & LSA

	Morphea	LSA
Epidermis	Normal	Atrophy of stratum malpighii
Follicular plugging	-	+
Hydropic degeneration of basal cells	-	+
Dermis	Homogenized	Marked edema
Subepidermal bullae	Infrequent	+
Elastic fibers	Present	Absent
Inflammation	+	-
Fibrosis	+	-

• Pathogenesis:

① it's an inflammatory condition caused by: incompletely defined Response to variety of- mechanical and antigenic stimuli

② these stimuli include: Trauma, Hormones spirochetal infection (Borreli Burgdorfei) autoimmune diseases

(3) LSA and Scleroderma → Represent: expression of the same antigenic insult with LSA → expressed in the papillary dermis

Scleroderma → in Reticular dermis and deeper

(4) Genetic predisposition:

associated with MHC class II antigen HLA-DQ7.

(5) Autoimmunity:

autoantibodies against extracellular matrix protien (ECM-1)

(6) Oxidative Stress:

lesion skin show: lipid peroxidation of epidemal Basal cell layers.
oxidative DNA damage
oxidative protien Damage.

• Treatment:

A Topical

1- Steroid → topical or intralesional

2- Topical Calcincurin inhibitors →
Pimecrolimus (1% cream) tacrolimus (0.1% ointment)

3- Vitamin A analogus 4- Vit D analogus

5- testosterone Topical or progesteron preparation → frequently used for tt of genital lichen sclerosus

B Systemic :-

1- Acitretin → help adult & Juvenile Cases
2- para-aminobenzoate → 12g daily
3- Anti-malarials → Hydroxychloroquine 250mg
4- Vitamin A + vit D analogues

C phototherapy :- effective

UVA-1 , PUVA < oral / Bath / cream , photodynamic Therapy

D Surgery :-

1- Circumcision in LSA of glans penis
2- Carbon Dioxide laser → for genital lesion in Both male - female
3- Vulvectomy → in SCC.

•Geriatric dermatology:•

•D.f:

Skin Diseases that are more Common in the geriatric population >65yr - Then in general popullion

Skin disorders common in the elderly

Eczemas	Infections
• Asteatotic eczema (xerosis). • Seborrheic dermatitis. • Contact dermatitis. • Stasis dermatitis (Fig. 9).	• Herpes zoster. • Candidiasis. • Onychomycosis. • Scabies.
Ulcers	Immunobullous
• Leg ulcers (Fig. 10). • Pressure ulcers.	• Bullous pemphigoid (Fig. 11).
Photodamage	Premalignant tumors
• Photoaging. • Solar elastosis.	• Actinic keratosis (Fig. 12). • Bowen's disease (Fig. 13).
Benign tumors	Malignant tumors
• Seborrheic keratosis (Fig. 14). • Skin tags. • Cherry angioma. • Sebaceous hyperplasia (Fig. 15).	• BCC (Fig. 16). • Lentigo malignant melanoma. • SCC (Fig. 17). • CTCL (Fig. 18).
Others	
• Senile purpura. • Senile pruritus. • Rosacea.	

• Aging - phstoaging •

[A] Intrinsic Aging:

- changes occuring in all individuals D.t normal maturity and senescence
- the underlying mechanism:- genetic - growth - Hormonal - mechanical factors
- Free Radicals: have a role By:
  - ↳ Direct Damaging effect on dermal fibers
  - ↳ or through induce alterations in the fibroblast functions
- Role of antioxidants:- vit C, E in preventing intrinsic ageing

[B] Extrinsic Aging:

- external agents: Chronic Sun Exposure (most impor (Dermatoheliosis)
- UVRs → induce tissue Damage By direct effect, generation of free Radical production of inflammatory cells

Cutaneous features of intrinsic & extrinsic aging

	Intrinsic aging "Sun-protected, innately aged skin"	Extrinsic aging "Actinically damaged skin"
Clinical features		
	Thin, smooth & lax skin.	Thick, rough, pale-yellowish skin (elastosis).
	Fine wrinkles.	Coarse wrinkles & furrowing.
	Graying of the hair.	Telangiectasia, irregularly pigmented, solar lentigo (liver spots), freckles, senile purpura, comedones, venous lakes, xerosis.
	Benign neoplasms.	Benign, premalignant & malignant neoplasms.
Histologic features		
Epidermis	Slight decrease in thickness.	Alternating atrophy & hypertrophy.
	Decreased corneocyte adhesion.	Thickened stratum corneum.
	Flattened rete ridges.	Thin granular layer.
	Reduplication lamina densa & anchoring fibril.	Marked dysplasia.
	Decreased no of melanocytes.	Increased no. & irregularly dispersed melanocytes.
	Decreased number of LCs.	Marked decrease in LCs number.
Dermis	Decreased thickness "atrophy".	Thickened.
	Decreased no. of elastic fibers.	Elastic fibers increase in no. & thickness. Tangled, densely matted & basophilic yellowish color of skin "dermal elastosis".
	Decreased no. of collagen fibers.	Marked decrease in collagen fibers.
	Decreased ground substance, with more heparin sulfate & less proteoglycans.	Ground substance: more glycosaminoglycans.
	Decreased vascularity.	
	Decreased fibroblasts.	
	Decreased mast cells.	
Subcutaneous tissue	Decreased especially face, hands & feet.	Non-specific changes.
Appendages	Decreased no. of eccrine glands.	
	Sebaceous gland hyperplasia.	
	Decreased no. of hair follicles.	

Age-associated skin changes & their possible explanations

Skin changes	Explanations
Poor wound healing.	• Fewer basal "proliferative" keratinocytes. • ↓ Epidermal turn-over time.
↓ Thermoregulation "↑ risk of heat stroke".	• ↓ Number of eccrine glands. • ↓ Vascularity.
Easy blistering of skin & tendency to pressure necrosis over bony prominences.	• Flattened DEJ. • ↓ Subcutaneous fat.
Increased risk of pressure, heat or chemical injuries. • ↓ Incidence & intensity of delayed hypersensitivity reactions, e.g. patch tests. • ↑ Risk of skin cancers. • ↑ Risk of infections.	• ↓ Sensory end organs • ↓ Cutaneous immune response. • ↓ Number of T-cells. • ↓ Number of LCs.
Easy bruisability.	• Atrophy of dermal ground substance, changes in collagen & elastic fibers. • Alterations in dermal vasculature
Xerosis "rough skin with fine white scales" → pruritus. ***Treatment:*** ↑ Humidity by a humidifier, mild soap (Dove®, Oil of Olay®, Oilatum®) & emollient application after bathing.	• Abnormal maturation & adhesion of keratinocytes. • ↓ Barrier function → ↓ water content. • ↓ Epidermal hyaluronic acid which is hygroscopic. • ↓ Eccrine functions. • ↓ Sebaceous lipids.
Contact dermatitis: More prolonged & persistent contact dermatitis.	• ↓ Dermal clearance of allergens & irritants. • "Muffled" inflammatory response.

• Atrophy of the Skin •

• D.F: Atrophy of the skin occur in many dermatoses

Produced By :- ↓↓ in the dermal Connective tissue.
(Collagen and elastic fibers)

- The skin is Smooth, thin with loss of elasticity.
- Atrophy that includes:
S.C tissue or deeper structures reffered to "Panatrophy"

• Anetoderma "Macular atrophy"

→ ch.ch By: Discrete atrophic patches The skin of which appear: Loose Thin, wrinkled, bulges slightly.

→ Types:

[I] primary :- arises on normal skin
⊖ Jadassohn - pellizzari type:
→ preceded by: inflammatory lesions
⊖ Schweninger - Buzzi Type: Not preceded By Inflammatory lesion.

[II] Secondary :-
- Relapces lesions of another disorders
- e.g :- Syphillis, LE, Leprosy, AV, TB, Urticaria Pigmentosa
Acrodermatitis Chronica atrophicans.

[III] Familial anetoderma.

• Causes of Cutaneous Atrophy:

① Congenital :-
- Aplastic Cutis
- Progeria
- Congenital poikiloderma
- Focal dermal Hypoplasia

② Acquired :-
→ Generalized: Aging - Rheumatoid disease - Steroid induced
→ Poikiloderma: → striae distensae → Anetoderma
→ Acrodermatitis chronica atrophicans → Atrophoderma
→ Atrophic Nevi → Panatrophy

✡ primary anetoderma :-

- rare disorder • female 20-40yr
- Crops:- of oval Erythematous Macules
- site: Trunk, thighs, Upper arms
- Gradually: each lesion fades → forming greyish white macules of wrinkled atrophic skin → Yeild on pressure, Can pushed inward easily by a finger.
- The number of lesions Varies: from 10 to 7200.

• Histopathology :-

1- At early stage:

• edema • perivasular - periappendegeal lymphocytic infiltrate (T-helper)

2- later:

The edema and infiltrate → subside & persistance of fine, irregular or twisted elastic fibers.

Collagen is usually normal.

• Pathogenesis :

- Focal elastolysis → D.t → Relase of elastase from inflammatory cells (present at early stage)
- infection or Complement activation OR Hormonal factors → play a role

• Treatment: Oral penicillin or antifibrinolytic drugs.

• Follicular Atrophoderma •

• lesion: dimple-like depression at the follicular orifices

• present: at Birth or early life.

• site: on the Back of Hand and feet.

- occur as: Isolated defect or associated e`:

Bazex S

- follicular atrophoderma
- Localized anhidrosis
- hypotrichosis
- multiple BCC.

Conradi's Syndrome

- X-linked dominant disorder • • Ichthyosiform erythroderma
- follicular atrophoderma
- Cataract
- patchy alopecia
- Calcific stippling of the epiphyses (Chondrodysplasia punctata)

palmo-plantar Keratoderma

• Keratosis pilaris atrophicans faciei "Ulerythema ophryogenes"

- lesion: Erythematous follicular papules healed e'i follicular atrophodermas.
- it involves: the lateral third of eyeBrows with some extension to the cheeks, peraurícular skin and forehead.
- appear: at or shoitly after Birth.
- more common: females 2nd, 3rd decades
- The condition Represent: atrophic variant of **Morphea**.
- **Borrelia Burgdoferi** → may involved
- **Histopathology**:
  - Thickening of the collagen bundles with Chronic perivascular inflammatory infiltrate in early lesions
- **treatment**:
  - none is effective
  - Antibiotic ttt (penicillin - oral tetracycline
  - Considered in early stages → with +ve Borrelia antibiotics

• Vermiculate atrophoderma "Folliculitis Ulerythematosa reticulata"

- Reticulate OR honey-comb type of atrophy that develop around horny follicular plugs on the cheeks

• Atrophoderma of pasini, Pierini.

- lesions: Round, oval, slightly depressed - slate-grey patches. with sharp "cliff-like" Border without induration
- site: commonly on the Trunk, mainly Back.

• Local panatrophy •

→ D.F: atrophy of skin, S.C fat, underlying muscles.
→ may be: variant of Morphea.
→ 2 Types:

Paratrophy of Glowers
- not preceded by inflammation
- No Scleroderma
- affect Back, Buttocks

Sclerotic paratrophy
- Preceded By: Sclerotic Changes

• Facial Hemiatrophy "Romberg's Syndrome"

→ D.F: gradual atrophy of skin, S.C tissue and muscle on one side of Face.
- Start out as → linear morphea
- later → become diffuse.

• Mid-dermal elastolysis.

• Pathogenesis: - defect in elastic fibers
D.t → Exposure to UV light
→ Autoimmunity
→ altered Balance Between matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinase TIMPs

• Clinically:
- Asymptomatic, Large, Diffuse area of Fine wrinkling → Following Cleavage Lines in the: Trunk, lateral neck, upper extremities
- Discrete perifollicular papules
- with the site of: the central hair follicle Being indented.

• Pathology:
1- Elastic tissue Stain → Verhoeff-van Gieson / Weigert's Stain
→ Selective loss of elastic fibers in mid dermis
2- with preservation of elastic tissue around the hair follicles → explain the Perifollicular papules
3- EM: phagocytosis of elastic fiber tissue By Macrophages

• Treatment: No effective ttt.

• Striae (S. distensae. S. atrophicans, Stretch marks)

• D.F: Breaks in the connective tissue → leads to Dermal atrophy
• Due to: - Hormones (Corticosteroids)
- mechanical stress
- genetic Predisposition
• lesion:-
1- initially: Red to violaceous elevated lines - mildly pruritic "Striae rubra"

2- over time:

The color gradually fades "Striae alba" and the lesion become → atrophic
è Skin surface → fine wrinkled appearance

- atrophic striae alba → permanent may fade over time.

3- atrophic Striae → may **Elevated** and "**Worm-like**" → in the setting of Severe edema (lymphedema)

4- Striae è systemic **Corticosteroids** and **Cushing's Syndrome**
Can be larger, more widely disturbed.

5- Flexural and intertriginous area → Develop from the use of Corticosteroid

- ingrills The most common sites:-
Thighs - hips - Buttocks - Breast
- in Boys: shoulders - Thigh - lumbosacral
- other less common sites:
abdomen, upper arms, Neck, axillae

Pregnant During Last Trimester. (11)

- **DD: Linear Focal elastosis** (elastotic striae)
- rows of yellow, palpable, striae-like Bands
- on the Lower Back
- Unlike Striae → the lesions are raised and yellow rather than depressed and white.
- Eldery men →
- Histologically → focal ↑↑ in the number of elongated or fragmented elastic fibers
as well as → Thickened dermis.
- its pustulated that linear focal elastosis → represent:- excessive regenerative process of elastic fibers
- viewed as:- Keloidal repair of striae distensae

• Treatment:-

1- Stretch marks tend to improve spontaneously over time

2- early stage Striae è tretinoin 0.1% cream

3- other topical tt:

0.05% tretinoin + 20% glycolic acid + 20% glycolic acid, 10% L-ascorbic acid

4- laser therapy:-
585 nm pulsed dye laser → for striae rubra.
improvement in the leukoderma of St. alba noted with 308 nm excimer laser

5- Carboxy therapy:

- to stimulate the production of local collagen
- CO_2 → has direct effect on fibloblasts which produce the collagen.

Disease	Clinical findings	Pathology	Associations
Anetoderma	Focal dermal defect: Localized areas of atrophic skin with laxity or herniated appearance over trunk, thighs & arms, ± overlying skin depressed or macular.	Normal epidermis, ↓ or absent elastic tissue in dermis with special stain (may appear normal on Hx & E), ± perivascular lymphocytes.	May be primary (idiopathic) or secondary (infection, inflammatory cutaneous disorder or tumor).
Atrophoderma of Pasini & Pierini	Single or multiple well-demarcated oval hyperpigmented patches with slight depression on back (most common) in young adults & adolescents. If linear following Blaschko's lines → **atrophoderma of Moulin.**	Minimal change including flattening of rete ridges, basal layer with ↑ melanin, ↓ dermal thickness, ± perivascular infiltrate.	Unclear if atypical atrophic form of morphea or separate entity; may be related to *B. burgdorferi*.
Mid-dermal elastolysis	Areas with diffuse fine wrinkling over trunk, upper arms &/or neck, ± preceding erythema.	Normal epidermis, selective loss of elastic fibers in mid dermis.	None.
Follicular atrophoderma	Dimple-like depression in follicular orifices consistent with ice-pick depressions on dorsal hands/feet or cheeks.	Dilated pore ± with underlying atrophy, often ↓ elastic fibers. If limited to cheeks → atrophoderma vermiculatum (Rombo syndrome, Nicolau-Balus syndrome).	Bazex syndrome Conradi-Hünermann-Happle syndrome.
Piezogenic pedal papules	Skin-colored papules in heels with pressure (due to herniation of fat), disappears when weight removed.	Fragmentation of dermal elastic tissue & herniation of fat into dermis.	Normal variant.

• perforating Dermatoses •

• **D.F:** groups of disorders in which altered components of skin are elliminated via the epidermis
By :- transepidermal ellimination

• Transepidermal ellimination TEE

- its the extrusion of foreign or altered domal components through the epidermis to the exterior with :- little or No disruption of the surrounding Structure.
- The extruded materials may be :- inflammatory cells, microorganisms, mucin or altered connective tissue components

"Aquired Reactive perforating Dermatosis"
ARPD :- suggested for these 4 primary perforating disorders when occuring in diabetes or in pt^ne chronic renal failure → undergoing Hemodialysis.

Disorders of transepidermal elimination "Perforating dermatoses"

Disorder	The eliminated material
Primary perforating disorders:	
Kyrle's disease	Collagen
Reactive perforating collagenosis	
Elastosis perforans serpiginosa	Elastic tissue
Perforating folliculitis	Necrotic material
Secondary perforating disorders:	
Granuloma annulare	Granulomatous process
Necrobiosis lipoidica diabeticorum	
Rheumatoid nodules	
Sarcoid	
Lichen nitidus	
Infectious granulomas, e.g. chromomycosis, TB, leprosy	
Pseudoxanthoma elasticum	Altered elastic tissue
Solar elastosis	
Chondrodermatitis nodularis chronica helicis	
Porokeratosis of Mibelli	Altered collagen
Intralesional steroid	
Calcinosis cutis	Calcified material
Osteoma cutis	
Myxoid cyst	Mucinous material
Alopecia mucinosa	
Papular mucinosis	
Cutaneous amyloidosis	Amyloid

Perforating epidermal disorders with transepidermal elimination

	Disorder	Clinical	Eliminated material	Treatment
1	**Kyrle's disease**	• Two forms: Idiopathic form & older diabetics with renal insufficiency. • Follicular & extrafollicular keratotic papules which may coalesce. • Can be generalized.	Granulomatous & basophilic debris including some degenerated collagen.	Topical & systemic retinoids.
2	**Perforating folliculitis**	• Young adults in second to forth decade & older diabetics on dialysis. • Multiple, widespread, follicular erythematous umbilicated keratotic papules. • Do not coalesce. • Köebnerization occurs.	Basophilic debris, degenerated collagen, eosinophilic elastic fibers, coiled-up hair in dilated follicle.	Topical retinoids.
3	**Elastosis perforans serpiginosa**	• Autosomal recessive pattern. • <30 yrs old. • Annular serpiginous lesions. • Idiopathic. • Reactive associated with heritable connective tissue disorders. • Penicillamine-induced.	Basophilic debris and elastic fibers into narrow epidermal channels.	Liquid nitrogen.
4	**Reactive perforating collagenosis**	• Inherited form in infancy & acquired in diabetes mellitus & renal insufficiency. • In trauma-prone areas köebnerization, pruritis in acquired type. • Umbilical keratotic papules.	Necrobiotic basophilic collagen bundles through epidermal perforation.	Avoidance of trauma, topical retinoids, PUVA.
5	**Perforating calcific elastosis**	• Very rare, more common in adult black women. • Keratotic papules involving the abdomen (periumbilical). • Associations: Multiparity, obesity and hypertension.	Calcified elastic tissue.	

★ Kyrle's disease ★ follicularis et parafollicularis

- D.F: rare disorder ch.ch By: { follicular / extrafollicular
  Red-Brown papules
  Containing: Central Keratotic plug
- They may enlarge to form: nodules
  or Coalesce → to form: verrucous plaques
- The limbs → most commonly affected
- may occur in pt ne: → DM / → chronic Renal F undergoing hemodialysis
- Histopathology + pathogenesis:-

-Parakeratotic column in an epidermal invagination Results when:
The Rapid rate of differentiation and keratinization → exceeds the Rate of proliferation
- The 1ry defect is: foci of vaculolated dyskeratotic cells
"Rapidly proliferating cells in Epidermis"

- when the keratotic plug → penetrates into Dermis → { inflammatory cells + Foreign Body cells } with Collagen degeneration occurs at this site.
- The eliminated materials is:- granulation tissue Basophilic debris which move upwards through Epidermal invagination
- Treatment:

Keratolytics - Cryotherapy - topical, systemic Retinoids

★ HyperKeratosis Lenticularis perstans "Flegel's disease"

- There is Asymptomatic flat Hyperkeratotic papules (smaller than Kyrle's disease)
- Located mainly: on the dorsa of the feet and Lower Legs

★ perforating Folliculitis ★

- ch.ch By: discrete Erythematous follicular papules → with contral Keratinous plug.
- mainly on :- the Extremities and Buttocks
- The lesion don't coalesce -
- ils described e` :- ↑↑ frequency in uremic diabetic ptns who Receiving Hemodialysis

- Histopathology:
  - Dilated follicle contains the elimanated material: → Basophilic debris
    - esinophilic elastic fibers
    - ortho, parakeratotic material
    - inflammatory cells
  - perforation are seen in the follicular infundibulum epithelium
  - The initation by the curled-up Hair → follicular hyperkeratosis and Retention of the Hair shaft in the follicle → BreakDown of follicular wall
- ††: Topical **tretinoin**

(To)

★ elastosis perforans serpiginosa ★ EPS

- D.F: Rare disorder ch.ch by: Small-Keratotic papules grouped in an annular or Serpiginous pattern e` an → atrophic, slight Hypopigmented center
  - mainly affect: The nape, side of Neck. arm - face - Trunk.
- Types 3:
  - → Idiopathic
  - → Reactive, associated e` CT disorders (PEX - marfan's syndrome, Down $)
  - → penicillamine-induced
- Associations: **MADD PORES.**

Marfan's **A**crogeria **D**own syndrome
D-pencillamine **P**seudo xanthoma elasticum
Osteogenesis imperfectia **R**othmund-Thomson
Ehlers Danlos **S**clerodema

- Histopathology:
  1. narrow. transepidermal canal that contain: necrotic material

- and Brightly esinophilic - degenerated el elastic fibers
- By elastic Stain:
  The dermis Contains an ↑↑ in the amount and thickness of elastic fibers
  "Pathognomic"
- the primary defect is: the abnormal elastic fibers → which act as a mechanical irritant to stimulate → epidemal Hyperplasia and → Canal formation with the extrusion of abnomal elastic fibers

● Treatment:
Liquid Nitrogen Freezing

★ Reactive perforating Collagenosis ★

● the lesion: small papules, gradually ↑ in size, → Become Umbilicated è a keratinous plug.
● they involute in: 6-10 weeks → leaving → Hypopigmented area or Slight Scar.
- New lesions → Continue to appear.
● Site: mostly in Trauma-prone areas e.g:
  → dorsal aspect of Hands
  → elbows - knees following superficial Trauma.
● Koebenerization is common.

2 types: → 1- inherited - autosomal Recessive accoring in infancy
→ 2- Aquired è DM, renal insufficiency

● Histopathology:-
Basophilic bundles of collagen → extending in vertical direction → extruded from the dermis Through → several areas of epidermal perforation

● Treatment:
- Avoid Trauma
- Topical Retinoids
- PUVA

Treatment of perforating diseases

Topical
• Retinoids (e.g. tretinoin, tazarotene).
• Corticosteroids.
• Menthol.
• Salicylic acid.
• Sulfur.
• Benzoyl peroxide.
• Emollients.
• Imiquimod.
Systemic
• Antihistamines (e.g. doxepin).
• Corticosteroids (intralesional, intramuscular, oral).
• Retinoids (vitamin A, acitretin, isotretinoin).
• Antibiotics (e.g. doxycycline, clindamycin, erythromycin, tetracycline, rifampicin).
• Methotrexate.
• Charcoal.
• Allopurinol.
Other
• Avoid trauma & scratching (wearing gloves, trimming of fingernails, behavior modification
trans- cutaneous nerve stimulator).
• Cellophane-tape stripping (for EPS).
• Phototherapy (broadband or narrowband UVB, PUVA).
• Cryotherapy.
• Electrosurgical destruction.
• Laser ablation (e.g. CO_2, Er:YAG, pulsed dye).
• Excision of larger bothersome lesions.
• Renal transplantation, if kidney failure.

★ Colloid Milium ★

- D.F: Degeneratie change ch.ch :- Small -Yellowish translucent papules
site: Sun exposed area.

3 types: ① Juvenile: Before puberty mainly on face.
② Adult: start in adult life affecting dorsa of the hands + face, neck
PF → Sun exposure
③ Nodular colloid degeneration: single or multiple Large nodules Not related to sun exposure

- Histopathology:
esinophilic - homogenous material in the Superficial dermis → Containing clefts with fibroblasts along the lines of cleavage.
- in adult Type:
Grenz Type Zone → Separate the epidermis from colloid masses
- pathogenesis:
- Juvenile Type colloid → of epidemal origin
- other 2 Types → demal origen
- Treatment: Dermabrasion - Cryotherapy

• FLushing •

• D.F : transient Reddening of the face frequently → other areas ⌈ neck, ears, upper chest

• Causes :

Widespread

① physiological
- emotions : anger, guilt
- Menopusal

② Drugs :
- Amyl nitrite
- Bromocriptine
- dipyridamole
- Histamine
- L-dopa

③ pathological :
- Carcinoid Tumor : intestinal - Bronchial
- pheochromocytoma

④ Zollinger-Ellisone $

⑤ Hereditary Angioedema

Localited

① physiological :
Triple Response : Reflex

② pathological :
- Urticaria
- Facial
  - Rosacea
  - Auriculotemporal $
  - sphenopalatine $
  - Ciliary neuralgia
- Acral :
  - Erythromelagia
  - Post-Raynaud's attacks

• pathogenesis :-

- ↑↑ Cutaneous Blood flow → occur Relaxation of Vascular Smooth muscles
- This occur via :

Autonomic nervous system
- è eccrine Sweating
- D.t direct effect on Both sweat glands and Blood vessels (Wet flush)

- Endogenous agents
- Vasoactive
- Histamine
- serotonin
- or Exogenous agents
- Not associated è ↑ sweating (Dry Flush)

• Treatment :

① Non-Selective β-Blockers : ← Nadolol, propranolol, Clonidine
effective in idiopathic flushing

② Anxiolytics :- helpful in emotional Symptoms or anxiety

③ in resistant troublesome Cases :-
Transthoracic endoscopic sympathectomy

Types of flushing

	Menopausal	Alcohol-induced	Carcinoid	Pheochromo-cytoma	Histamine induced
Pathogenesis	• Estrogen lack. • Menopause. • Oophorec-tomy.	• Direct effect of alcohol. • Vasodilation from acetal-dehyde (in al-cohol dehy-drogenase de-ficiency). • Vasoactive substances, e.g. tyramine. • Chloropropa-mide. • Antabuse.	• Kinins. • Tumor of foregut, hindgut, lung, ovary, pancreas.	Catecholamine production by tumor of adrenal medulla, acces-sory adrenal tis-sue, glomus jugulare.	• Hista-minemia. • Urticaria pigmentosa. • Systemic mast cell disease. • Wine (histamine content).
Provocative factors	Spontaneous	Alcohol	• Alcohol • Over-breathing. • Nor-adrenaline.	Spontaneous.	• Certain wines. • Codeine.
Distribution	Head, neck, chest	Head, neck, chest	Face, neck, trunk, arms, legs.	Face, neck, chest, trunk.	Face, neck, chest, limbs.
Duration	5-15 mins.	15-30 mins.	15 mins to 4 hrs.	15 mins to 4 hrs.	15 mins to 2 hrs.
Associated features	• Hyperhidrosis. • Tremulous. • Depression.	Urticaria, pruritus.	• Diarrhea, abdominal pain. • Asthma.	• Hyperhidrosis. • Piloerection. • Hypertension.	Headache.
Investigations					
Urine	Pituitary gon-adotropin ↑.		5-Hydroxy-indoleacetic acid (5-HIAA).	Vanillylmandelic acid (VMA).	Histamine +.
Treatment	Estrogens (hormone re-placement therapy), clonidine or (SSRIs).	Avoidance of chemicals or drug exposure.	Surgical	Surgical	Anti-histamines.

DD of red face (Figs 29-33)

- Flushing disorders.
- Rosacea.
- Dermatitis:
  - Atopic.
  - Contact/photocontact.
  - Seborrheic.
- CT diseases:
  - LE.
  - Dermatomyositis.
- Photogenodermatoses:
  - Xeroderma pigmentosum.
  - Cockayne syndrome.
  - Bloom's syndrome.
- Photometabolic:
  - Porphyria (erythropoietic – Gunther).
  - Hartnup disease.
- Erysipelas.
- Physical erythemas:
  - High temperature (burns).
  - Low temperature (frost-bite).
  - UVR.
- Chronic actinic dermatitis.
- Cutaneous lymphomas.

Clinical approach to the evaluation of flushing

Identify provocative factors:

- Direct questioning.
- Patient diary (food, medications, activities).

Check for associated symptoms:

- Sweating.
- Urticaria.
- Diarrhea.
- Bronchospasm.

Investigation (not required in all cases):

Indicated if flushing:

- Of sudden or recent onset.
- Severe.
- Associated with systemic symptoms.

Investigations to consider:

- Complete blood count with differential & platelets.
- Thyroid function tests.
- Serum tryptase, histamine &/or chromogranin A levels; plasma free metanephrines.
- 24-hour urine collection for:
  - Serotonin metabolites such as 5-hydroxyindole acetic acid (5-HIAA).
  - Fractionated metanephrines.
  - Histamine metabolites such as methylimidazole acetic acid (MIAA).
- CT/MRI scans, somatostatin receptor scintigraphy (using radiolabeled analogue of somatostatin).

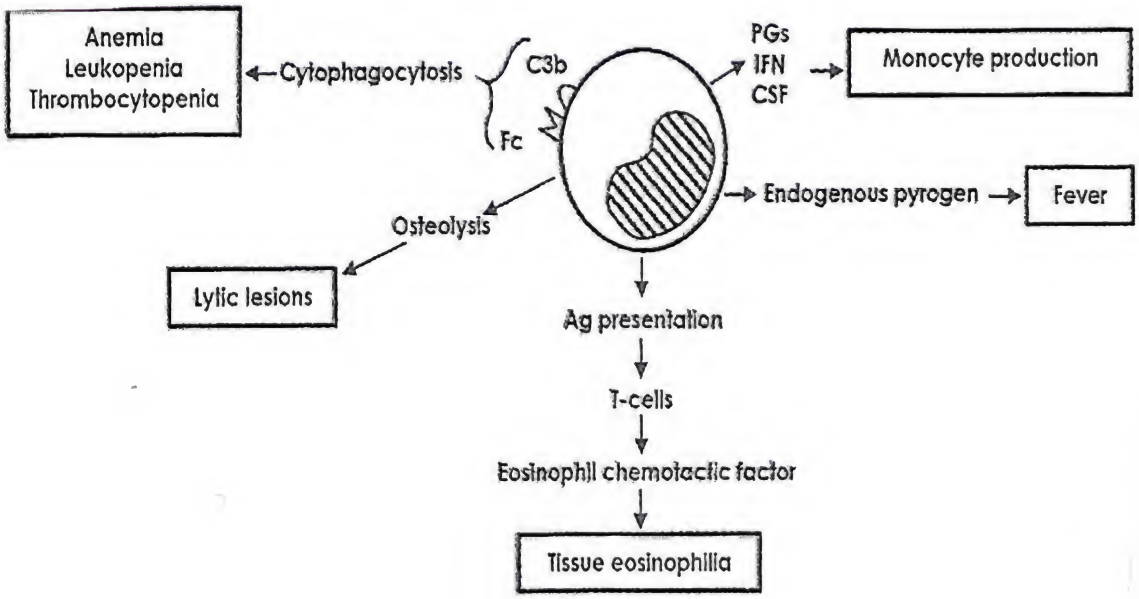
Elimination:

- Exclude suspected drugs & food additives.

• Histiocytoses •

• Def: Heterogenous groups of diseases ch.ch By: accumulation of reactive or neoplastic histocytes in tissue.

- The clinical picture is d.t :-
  The functional activity of these cells and their abnormal Regulation



• Class 1: Langerhans Cell Histiocytosis

→ Disease of unknown cause
→ Ch.ch. By: Proliferation of Langerhans histocytes
→ includes:- 4 clinical forms :-

1 ACute disseminated LCH letterer Siwe :-
- occur during the first year of life with fatal Viscoral involument

Systemic signs
- fever
- anemia
- Hepatosplenomegaly
- lymphadenopathy
- pulmonary infiltrate
- Osteolytic lesions

Cutaneous lesion
- 80% 1st sign
- closely set Brown scaly papules :-
  Resembling → Seb. dermatitis
  → Darier Dis
- Petechiae - purpura
- site: scalp - flexural areas - Trunk

2P

2 Chronic multifocal LCH:

[Hand-Schuller-christian-Disease]

- occur during: Early Childhood (2-6yr)
- with predominantly osseous lesion
- less extensive visceral affection.
- Triad:
  - diabetes insipidus
  - Exopthalmos (10%)
  - multiple Bone defect (skull)
- May occur:
  - Hepatosplenomegaly
  - pulmonary infiltrate
  - lymphadenopathy
- Cutaneous lesions 30%
  - Ulcerated plaques — axillae, mouth, genitalia
  - Seborrheic-like dermatitis
  - rarely → papular xanthomas
  - infant è Crusted purpuric papules

\+

seborrheic like eruption in [scalp, groin]

↓

Should raise the suspicion of

LCH

3 Benign Localized (esinophilic granuloma of Bone)

- most common and least sever forms of LCH
- occur in: Older children + Adults
- solitary or few lesions of Bones
- rarely Cutaneous lesions occur

4 Congenital self-healing reticulohistiocytosis:

[Hashimoto-pritzker disease] HPD

- Benign - self healing variant - Present at Birth.
- multiple, disseminated - firm, Reddish-Brown nodules → heals later on → leaving: whitish atrophic scars.
- Absence of mucous membrane lesions and systemic signs → Key features

---

- Histopathology:-
- All Types è typical "LCH cell" → easily identified
  - large with irregular-vesiculated-Kidney Shape nucleus
  - Abundant cytoplasm

*in Letter-Siwe:-

there is proliferative reactions with an infiltrate formed of LCH cells in upper dermis → invades the epidermis

✱ In Hand-Schuller-Christian disease

- There is xanthomatous Reaction e` groups of foam cells in the upper dermis
- intermingled with LCH cells. and eosinophils
- Multi-nucleated giant cells → frequently present mainly of the foreign-body Type But occasionally have the appearance of Touton giant cells

✱ In eosinophilic granuloma :-

- there is granulomatous reaction with extensive aggregates of LCH and **Clusters** of eosinophils and **giant cells**

✱ In Hashimoto pritzker disease :

- the LCH cells are intermingled with Large multinucleated giant cells in mid or deep dermis

= Histiogenesis :-

- EM studies : 50% of LCH cells Contain Birbeck's granules of LCs

- LCH cells :-
  - +ve immunostaining for CD1a . Langerin (CD207, S100)
  - ATpase → peanut Lectin, α-mannosidase → +ve in LCH cells.
  - Staining for these is less effective performed as CD1a staining → more specific.
  - Don't express Factor XIIIa (marker of Type I dendrocytes) or classic macrophage / monocyte markers :-
    - ↳ CD68
    - ↳ HAM56
  - Markers capable of distinguishing LCH cells from LCs of normal skin :
    - peanut agglutinin (PNA
    - IFN-α Receptors
    - Placental alkaline phosphatase (PLAP)
  - Human Herpes virus (HHV) type 6 → may play arole in the pathogenesis of LCH
  - **Langerin** → Highly specific Langerhans cell marker Because its the major protien of Birbeck granules
- Definite Diagnosis Require :-
  - → +ve CD1a stain or electron microscopie demonstrate of Birbeck granules

Treatment of Langerhans cell histiocytosis

Single-system disease			Multisystem disease
Skin		Bone	
Children	Adults		
• Observation or topical nitrogen mustard.	• Topical nitrogen mustard. • PUVA. • CO_2 laser. • Thalidomide. • Isotretinoin.	• Surgery. • Glucocorticoid injections. • Radiotherapy. • Monochemotherapy (in multiple bone lesions).	• Monochemotherapy with vinblastine or etoposide, preceded or not by glucocorticoid administration. • Non-responders may be treated with polychemotherapy.

Class II : Non-LC Histiocytosis

JXG ① Juvenile Xanthogranuloma

- Most Common form of Non-LC histocytosis
- male → Childhood - Adult → equal sex

⭐ Cutaneous lesions :-

- Clinically: Firm, rubbery, yellowish papules or nodules at Birth or early infancy.
- Site: mainly head - neck
- Involute → spontaneously within 3 - 6 yrs
- 2 clinical variants:
  - ↳ numerous small papular form
  - ↳ large nodular form

- Involvement of: Oral M.M may occur → Ulceration, Bleeding mainly on → lateral aspect of tongue + midline of Hard palate
- Unusual presentation:
  - ↳ Unusual clinical lesions → Hyperkeratotic, pedunclated lesions
  - ↳ Unusual sites → penis - toe - nail - lip - Scrotum
  - ↳ Unusual size → multiple giant form

⭐ Extracutaneous manifestations

Iris → Hge in anterior chamber → Uncontrolled Glaucoma

other sites :- Lung • hepatomegaly testicular swelling, pericardial effusion → all may go: Spontenous Remission

⭐ Association

- ↳ Cafe-au lait spots ↳ Neurofibromatosis NF
- ↳ Childhood leukemia
- ↳ Triple: JXG + NF1 + JCML

Histopathology:

- Dense well demarcated Histiocytic infiltrate within papillary dermis
- Cellular infiltrate → histocytes e- vacuolated Cytoplasm
  → Touton giant cells
  (e- complete circle of nuclei around Homogenous esinophilic cytoplasm)
- Foamy Cytoplasm → seen outside the circle of nuclei)
  → lymphocytes
  → esinophils - Neutrophils

Ultrastructure:

- Histocytes è an irregular nucleus Rich in → pseudopods
  → lysosomal structure
  → dense Bodies
- Clusters of Comma-shaped Bodies Can Observed
- But → Birbeck granules Absent

immunoHistochemistry :-

- proliferating histocytes → -ve for CD1a and Langerin CD207
  → +ve for HAM56 CD68, factor XIIIa

Treatment:

1- No treatment → self-limiting lesion
2- Excision for diagnostic or Cosmotic reasons
3- Early ttt of Uveal lesions e.g: Steroids
4- Systemic lesions → Chemotherapy
   → Steroid, Cyclosporine
   (only if interfering e- vital function)

Approach to ptnè JXG

- Solitary lesion → easily diagnosed clinically
- multiple lesions → require skin bioPsies
- General, Systemic examination → to detect extra Cutaneous involvement
- Opthalmological follow up → every 6 months for those e- Ocular lesion

② Papular Xanthoma PX

- lesion: → generalized, yellowish asymptomatic papulonodular
- No tendency to merge into plaques
- No visceral affection
- Normal Lipid profile
- Absent diabetes insipidus.
- **Histopathology:**
  - Composed entirely of:-
    - Foamy cells
    - Touton giant cells

③ Necrobiotic Xanthogranuloma

NXG
→ ulcerated yellowish plaques
→ mainly in: periorbital area
→ associated w:-
- paraprotinemia (90%)
- Cryoglobulinemia 40%.

- **Histopathology:**
  - Granulomatous infiltrate → involving the whole dermis and subcutis
  - formed of → lymphocytes → Foamy cells
    → Epitheliod cells → Touton giant cells
  - area of: clearly defined severe Necrobiosis.

④ Benign Cephalic Histiocytosis:-

- lesion: self healing - Yellowish papules
- Localized in: Face of infants (14 month old)
- Histopathology:

well-circumscribed Histocytic infiltrate (clusters of comma shaped Bodies by EM) → closely attached to Epidermis

⑤ Xanthoma Disseminatum:-

- Occur in: Adults
- lesion: orange or yellowish-Brown papules and nodules - widely disseminated
- mainly on: flexor surfaces → neck, axilla, groin - perianal
- The Mucous membrane → Commonly affected 50%.
- Yellowish nodules → in pharynx and larynx
  Horseness - Dyspnea.

- DM → in 50% of ptns
- Histopathology :

Early → large Histocytes
Late → foam cells (xanthoma cells)
Numerous → Touton giant cells and inflammatory infiltrate
- may be a variant of →
Hand-Shuller-Christian disease.

- Treatment:

- Systemic steroid
- DI → Vasopression

⑥ Multicentric Reticulo-Histocytosis (MRH)

- Rare, histocytic, proliferative disease ch.ch By:

↳ ① polyarthritis: (60%)
affecting: Hands, precedes the lesion
↳ ② Skin lesions:
Firm-Brown-Yellow papules
affecting: extensor surfaces of-
The Hands - forearm - pruritis 25%.
↳ ③ mucosal involvement: 50% (mouth-lip-tongue)
↳ ④ Abnormalities of Serum lipids: 30%
↳ ⑤ associated internal malignancy 20%
gastric - Ovarian - Breast Carcinoma - myeloma. melanoma - lymphoma

- Histopathology:

Infiltration By mono- and multi-nucleated giant cells with voluminous ground glass cytoplasm

- EM Study:

Type IV collagen inclusions

- Immuno-cytochemically: histocytic phenotype (+ve for ATpase, lysozyme, α-1 anti-trypsin)

- Treatment:

systemic steroids alone or ē Azathioprine.

⑦ Diffuse normolipemic plane Xanthoma

DPX
- lesion: Diffuse yellow patches in periorbital area, upper trunk.
- may arise in; association ē
  - multiple myeloma
  - erythroderma
  - leukemia
  - paraprotinemia
- Normal serum lipid
- Histopathology: sheets of foam cells, Touton giant cells

(8) Histiocytoma

[Progressive nodular histiocytoma]

- Chronic Brown - Firm nodules
- Site: Lower extremities
- Persist for many years
- Conjunctival, Oral, laryngeal lesions may occur.
- Histopathology:

Early:
- accumulation of Xanthomatized and Scalloped histiocytes
- Some infiltrating lymphocytes

Older lesion
- Spindle shape Histiocytes
- arranged in Storiform pattern
- occasional giant cells → present

- Cells +ve CD68 and Factor XIIIa
  - ve → for S100 + CD1a.

[Generalized eruptive Histiocytoma]

- Eruptive flesh-colored papules → Develop in Crops → Involutes Spontaneously
- Histopathology:
- Proliferation of monomorphic histiocytes Cells in the upper and mid dermis
- No giant cells or foam cells are present
- Scattered lymphocytes → many present

Class III: Histiocytosis

Malignant Histiocytosis

Histiocytic Medullary Reticulosis

- occur in Children or Adults
- with prognosis within few months
- Rare → Histiocytic Proliferative disorder with
  - Acute onset
  - Fever, lymphadenopathy - Pancytopenia
  - Hepatosplenomegaly - Jaundice purpura
- Cutaneous lesion:
  - Specific 10%.
  - more in children
  - Papules-Nodules - plaques → Ulceration
- Histopathology:
  - middle - lower dermis → masses of normal and atypical Histiocytes (Large Vesicular Nuclei + phagocytosed Erythrocytes)

+nuclear debris and fragments of leucocytes in their Cytoplasm)

-with focal areas of necrosis and acute inflammation

- **DD:-**

-Prominent erythrophagocytosis

Diffrentiate From Hodgkin's disease and Letterer-Siwe Disease

- **treatment:**

- Combined chemotherapy.

e.g: Cyclophosphamide
prednisolone - vincristine
splenectomy

Classification of the histiocytoses

Class I (Langerhans cell histiocytosis "histiocytosis X"):

- Letterer-Siwe disease.
- Hand-Schuller-Christian disease.
- Eosinophilic granuloma.
- Self-healing reticulohistiocytosis (Hashimoto-Pritzker disease).

Class IIa (dermal dendrocyte histiocytosis):
The predominant cell is the dermal dendrocyte (positive for CD68 & factor VIIIa) & the typical histological change is a xantho-granulomatous reaction.

- JXG.
- Benign cephalic histiocytosis.
- Erdheim-Chester disease.
- Generalized eruptive histiocytoma.
- Fat-storing hamartoma of dermal dendrocytes.
- Papular xanthoma.
- Progressive nodular histiocytosis.
- Xanthoma disseminatum.
- Diffuse plane xanthomatosis.

Class IIb (non-Langerhans & non-dendrocytes histiocytosis):

- Reticulohistiocytoma.
- Multicentric reticulohistiocytosis.
- Familial hemophagocytic lymphohistiocytosis.
- Familial sea-blue histiocytosis.
- Hereditary progressive mucinous histiocytosis.
- Malakoplakia.
- Necrobiotic xanthogranuloma.
- Sinus histiocytosis with massive lymphadenopathy.
- Virus-associated hemophagocytic syndrome.

Class III: Malignant histiocytic disease.

- Monocytic leukemia.
- Malignant histiocytosis (may be of the mononuclear phagocyte, Langerhans' cell or dendrocyte cell type)
- Histiocytic lymphoma (may also be of the mononuclear phagocyte, Langerhans' cell or dendritic cell type).

Clinical features of the histiocytoses HL

Histiocytosis	Usual age	Most common mucocutaneous sites	Other findings
Langerhans cell histiocytoses			
Letterer-Siwe disease	0-2 yrs	Scalp, flexural areas, trunk.	Visceral & bone lesions.
Hand-Schüller-Christian disease	2-6 yrs	Scalp, flexural areas, trunk, gingival.	Diabetes insipidus, bone lesions, exophthalmos.
Eosinophilic granuloma	7-12 yrs	Skin lesions rare.	Bone lesions primarily.
Congenital self-healing reticulohistiocytosis (Hashimoto-Pritzker disease)	Congenital	Widespread, localized or single lesion.	Spontaneous resolution, but children should be followed longitudinally.
Non-Langerhans cell histiocytoses			
Primarily cutaneous, usually self-resolving			
Juvenile xanthogranuloma	0-2 yrs	One to a few lesions >> numerous & widespread. Head and neck > upper trunk > extremities	Rare eye & visceral lesions; spontaneous resolution; association with CALM, NF-1 &/or juvenile myelomonocytic leukemia.
Benign cephalic histiocytosis	0-3 yrs	Face & neck > trunk & extremities.	Usually none (diabetes insipidus rare); spontaneous resolution.
Giant cell reticulohistiocytoma	Adults	Head (solitary lesion).	None; spontaneous resolution.
Generalized eruptive histiocytoma	<4 & 20-50 yrs	Widespread (axial)	Recurrent crops; spontaneous resolution.
Indeterminate cell histiocytosis	Any	Solitary or generalized. Trunk & extremities > head & neck, genitalia.	Uncommon visceral & bone lesions; possible association with B-cell lymphoma & leukemia.
Primarily cutaneous, often persistent/progressive			
Papular xanthoma	Any	Generalized (discrete yellow papules & papulonodules with relative sparing of flexural sites).	Mucous membrane involvement can occur occasionally.
Progressive nodular histiocytoma	Any	Generalized (discrete yellow papules & nodules, sometimes with prominent facial involvement).	May represent same entity as the progressive form of papular xanthoma; mucous membrane involvement can occur.
Hereditary progressive mucinous histiocytosis	Childhood / adolescence	Generalized (skin-colored to erythematous papules & nodules).	Usually occurs in female patients; histologically, abundant dermal mucin in addition to histiocytes.

Clinical features of the histiocytoses *(Cont'd)*

Histiocytosis	Usual age	Most common mucocutaneous sites	Other findings
Cutaneous, with frequent systemic involvement			
Necrobiotic xanthogranuloma	17-60 yrs	Periorbital > other face, trunk, extremities.	Paraproteinemia due to plasma cell dyscrasia or lymphoproliferative disorder, hepatosplenomegaly.
Multicentric reticulohistiocytosis	30-50 yrs	Head, hands, elbows (over joints), mucosa (oral, nasopharyngeal).	Arthritis (often destructive), up to 30% with internal malignancy.
Rosai-Dorfman disease	10-30 yrs	Eyelids & malar area.	Massive lymphadenopathy in a subset of patients, fever, hypergammaglobulinemia, skin-limited form increasingly recognized.
Xanthoma disseminatum	Any	Flexural areas to widespread>mucosa (oral, nasopharngeal).	Diabetes insipidus.
Systemic, with skin involvement rare to unusual			
Erdheim-Chester disease	Any	Skin involvement ~25% of patients: eyelids, scalp, neck, trunk, axillae (red-brown to yellow nodules & indurated plaques).	Fever, bone lesions, exophthalmos, diabetes insipidus, involvement of the lungs, kidneys, adrenals, heart, CNS, retroperitoneum & testes; high mortality rate.
Sea-blue histiocyte syndrome (sea-blue histiocytosis) • Inherited • Acquired	Usually adolescence/ young adulthood (inherited form)	Skin involvement rare (inherited form): Facial (macular hyperpigmentation & nodules).	Histiocytes contain cytoplasmic granules that stain azure blue with May-Grünwald stain; multiple organs involved; can be fatal.

Adapted from: Bolognia et al., Dermatology Textbook. Third edition, 2012.

Primary Immunodeficeincy • Disorders •

- Represent: Helerogenous group of inherited disorders
- Ch.ch By: immune System defect that Result in → Susceptibility to infections as well as → additional manifistations
  Sus has: → aut oimmunity
  → allergy
  → malignancy
- ptn è genetic immunodeficiency Disorders → manifist e' Cutaneous abnormalities
- Some of these skin finding are Highly ch.ch of particular disorder
- others as:- eczematous OR granulomatous Dermatitis → are shared By othe immunodeficiency

• Causes of 1ry immunodeficancy:

① disorder of cell-mediated immunity:
→ Sever combined immunodeficancy (SCID)
→ MHC antigen deficancy (class I, class II)
→ other combined immunodeficancy:-
- DiGeorge anomaly
- Wiskott-Aldrich Syndrome.
- X-linked Hyper IgM &
(autoimmune lymphoproliferative syndrome)

② DNA Repair defect:
- Xeroderma pigmentosum
- ataxia telangiectasia
- Bloom's Syndrome
- Fanconi's anemia.

③ Defect of antibody production:
- X linked agammaglobulinemia
- IgA deficiency

④ Disorders of phagocytic cells:
- chronic granulomatous disease
- Neutropenia
- Hyper-IgE syndrome
- leukocyte adhesion Disorder

⑤ Complement disorders: deficiencies

⑥ other immunodeficiency:
- Anhidrotic ectodermal dysplasia
- Incontinentia pigmenti
- Dyskeratosis Congenita
- Papillon-lefevre Syndrome.

• Causes of 2ry immunodeficiency:

[1] infections:
- Viruses → HIV - HBV - measles - Rubella
- Bacterial → sepsis - Tuberculosis
- Parasitic + protozoal infection

[2] Drugs:
- Immunosuppresive Drugs: - Corticosteroids - Cyclophosphamide
- Biologicals: Anti-TNF, anti-CD3 - anti CD4
- Anticonvulsants: phenytoin - Carbamazepine
- Physical therapy: irradiation, plasmapheresis
- Malignancy: lymphoma - leukemia - Myeloma
- Metabolic: DM - chronic Renal Failure, Nutritional deficiency
- Miscellaneous: Burns - toxins

[3] alcohol - cigarrates - extremes of age.

Test	Finding	Immunodeficiency identified
Complete blood count with differential, platelet count & examination of smear	• Giant granules within neutrophils, ± neutropenia. • Neutrophilia. • Small platelets, thrombocytopenia.	• Chédiak-Higashi syndrome. • Leukocyte adhesion deficiency. • Wiskott-Aldrich syndrome.
Hair shaft examination	• Small, regular clumps of melanin. • Large, irregular clumps of melanin.	• Chédiak-Higashi syndrome. • Griscelli syndrome (type 2; RAB27A).
Quantitative immunoglobulins	• All Ig↓ • IgA↓, IgG↓, ± IgM↓ • IgA↓ or IgM↓ • IgM↑, all other Ig↓ • IgM↑, ± IgA↑, ± IgG↓ • IgA↓, IgE↓, $IgG_{2,4}$↓ • IgE↑↑ • IgM↓, ± IgG↓, IgA↑, IgE↑	• X-linked agammaglobulinemia. • Common variable immunodeficiency. • Selective IgA or IgM deficiency. • Hyper-IgM syndrome. • Hypohidrotic ectodermal dysplasia with immunodeficiency. • Ataxia-telangiectasia. • Hyper-IgE syndrome. • Wiskott-Aldrich syndrome.
Total hemolytic complement (CH50)	• Marked ↓	• Various complement deficiencies.
Nitroblue tetrazolium (NBT) reduction assay	• <10% of normal NBT reduction.	• Chronic granulomatous disease.
T- & B-cell analysis by flow cytometry	• Lack of T-cells ± B-cells.	• Severe combined immunodeficiency.

Miscellaneous

- Management of metabolic complications of erythroderma. (2012).
- Etiology and management of a case of erythroderma. (2007).
- Erythrodserma: causes, d.d, complications, ttt . (2008).
- Definition and causes of face flushing. (2010).
- How to approach a case of perforating dermatoses. (2010).

differential diagnosis of erythematous eruption in the crural area (2001).
differential diagnosis of chronic oral ulcers (2001).
outdoor swimming pool related dermatoses (2001).
hand, foot and mouth disease (2001).
uveitis (2000).
the diagnostic approach to big toe nail hyperpigmentation (2000).
palmoplantar keratoderma (2000).
differential diagnosis of white patch of oral mucosa (2000).
differential diagnosis of annular erythema (1999).
temperature dependent skin disorders (1999).
insufficient or unbalanced food intake may have dermatological sequelae. Discuss the statement (1999).

Cutaneous findings in primary immunodeficiency disorders

Disorder	S. aureus infections		CMC	Warts	Eczematous dermatitis	Granulomatous dermatitis* (non-infectious)	LE	SVV	Ulcers (PG-like)	Other findings
	Superficial pyodermas	Abscesses								
Ataxia-telangiectasia	+	+			+	+ (often ulcerate)				Oculocutaneous, telangiectasias, progeric changes, CALM, BCC.
Chédiak-Higashi syndrome	+	+							+	Pigmentary dilution, hyperpigmentation in sun-exposed sites, silvery hair, bleeding diathesis, gingivitis.
Chronic granulomatous disease	++	++	+		+	++ (nodular, necrotic)	+		+	DLE in female carriers, Sweet's syndrome, oral ulcers
Chronic mucocutaneous candidiasis			++			++ (candida)				Dermatophyte infections, vitiligo, alopecia areata
Common variable immunodeficiency	+	+	+	+	+	++	+	+	+	Dermatophyte infections, vitiligo, alopecia areata
Complement deficiencies	+	+	+				++	+	+	Dermatomyositis, urticaria, lipodystrophy (C3), JIA
DiGeorge syndrome†			+		+	+				
Hyper-IgE syndrome	++	++ (cold)	+	‡	++					Neonatal papulopustular eruption
Hyper-IgM syndrome	+	+		+		+	+		+	Oral ulcers
Idiopathic CD4+ lymphocytopenia			+	++			+			
IgA deficiency	+	+	+		+		+	+	+	Vitiligo, lipodystrophia centrifugalis abdominalis

Cutaneous findings in primary immunodeficiency disorders *(Cont'd)*

Disorder	S. aureus infections		CMC	Warts	Eczematous dermatitis	Granulomatous dermatitis* (non-infectious)	LE	SVV	Ulcers (PG-like)	Other findings
	Superficial pyodermas	Abscesses								
IgM deficiency	+	+		+	+		+			
IL-1 receptor-associated kinase-4 (IRAK-4) deficiency	++	++ (cold)	+							
Leukocyte adhesion deficiency		++ (necrotic)							++	Poor wound healing, delayed separation of the umbilical stump, gingivitis
SCID	+	+	+	+	+	+*				GVHD, erythroderma (Omenn syndrome)
TAP deficiency						++		+	+	
WHIM syndrome	+	+		++						
Wiskott-Aldrich syndrome	++	+			++	+		+		Bleeding diathesis
X-linked agamma-globulinemia	+	++			+	+				Dermatomyositis-like eruption (due to echovirus); ecthyma gangrenosum

** Extensive cutaneous & extracuatneous granulomatous disease (including destructive midfacial granulomas) has been described in children with hypomorphic RAG1 or RAG2 mutations.*

† Defective thymic function, hypocalcemia secondary to hypoparathyroidism, congenital heart defects, & craniofacial anomalies, due to 21q11 deletions.

‡ Patients with autosomal recessive forms of hyper-IgE syndrome are also at increased risk of developing mucocutaneous squamous cell carcinoma & severe warts, molluscum contagiosum & herpes simplex or varicella-zoster viral infections.

+, occasional findings; ++, common finding; BCC, basal cell carcinoma; CALM, café-au-lait macules; CMC, chronic mucocutaneous candidiasis; DLE, discoid lupus erythematosus; GVHD, graft-versus-host disease; IL, interleukin; JIA, juvenile idiopathic arthritis; LE, lupus erythematosus; PG, pyoderma gangrenosum; SCID, severe combined immunodeficiency; SVV, small vessel vasculitis, TAP, transporter associated with antigen processing; WHIM, warts, hypogammaglobulinemia, infections & myelokathexis.

Bolognia et al., Dermatology Textbook, Third edition, 2012.

Miscellaneous

- Management of metabolic complications of erythroderma. (2012).
- Erythrodserma: causes, d.d, complications, ttt . (2008).
- Definition and causes of face flushing. (2010).
- How to approach a case of perforating dermatoses. (2010).
- Non infectious pustular lesions of skin in adult. (2009).
- Differential diagnosis of an erythematous plaque on the face (2006).
- Differential diagnosis of erythroderma in infancy and childhood (2004 - 1990).
- Differential diagnosis of papular eruption on the face (2003).
- Red Baby (2003).
- Dermatologic conditions that may affect man from cats (2003).
- Differential diagnosis of erythema on the face (2003).
- Skin diseases caused or aggrevated by exposure to cold (2002).
- Differential diagnosis of hyperpigmented patches of the cheeks (2002).
- Give short account of microabscesses in different skin lesions (2001).
- Differential diagnosis of skin colored papular eruptions around eye (2001).

36

- Etiology and management of a case of erythroderma. (2007).
- Erythrodserma: causes, d.d, complications, ttt .

- Differential diagnosis of erythematous eruption in the crural area (2001).
- Differential diagnosis of chronic oral ulcers (2001).
- Outdoor swimming pool related dermatoses (2001).
- Hand, foot and mouth disease (2001).
- Chelitis (2000).
- The diagnostic approach to big toe nail hyperpigmentation (2000).
- Palmoplantar keratoderma (2000).
- Differential diagnosis of white patch of oral mucosa (2000).

37

- Differential diagnosis of annular erythema (1999).
- Temperature dependent skin disorders (1999).
- Insufficient or unbalanced food intake may have dermatological sequalae. Discuss the statement (1999).
- Differential diagnosis of brownish black maculopapular lesion less than 1 cm in diameter on the cheek in an adult male (1999).
- The nail changes as a manifestation of dermatological conditions (1999).
- Pustular eruption in neonates (1997).
- Differential diagnosis of ulcers and erosions of the mouth (1996).
- Circumscribed area of loss of scalp hair: discuss how to arrive at the diagnosis of a case of (1994).